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Metacarpophalangeal Pattern Profile Analysis in Sotos Syndrome

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Abstract

The metacarpophalangeal pattern profile (MCP) was analyzed on 16 Sotos syndrome patients. A mean Sotos syndrome profile was produced. Correlation studies confirm clinical homogeneity of Sotos syndrome individuals. Discriminant analysis of Sotos syndrome patients and normal individuals produces a function of two MCP variables and age, which may provide a useful tool for diagnosis.

Keywords

Sotos syndrome; metacarpophalangeal pattern profile (MCP); discriminant analysis; correlation studies

INTRODUCTION

Sotos syndrome, or cerebral gigantism, was first described by Sotos et al [1964]; at least 100 cases were reported subsequently. This syndrome is characterized by large size at birth, large hands and feet, advanced osseous maturation, macrocephaly with prominent forehead and

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mild dilatation of lateral ventricles, down-slanting palpebral fissures, hypertelorism, prognathism, abnormal coordination, and variable degrees of mental retardation and language deficits, although retardation is not always present [Bloom et al, 1983]. Most are sporadic cases, although autosomal recessive and dominant inheritance has been suggested [Halal, 1982]. Early diagnosis is difficult; therefore, quantitative methods based on clinical characteristics may be helpful.

Metacarpophalangeal pattern profile (MCP) analysis is an evaluation of the hand skeleton based on a comparison of 19 tubular bone lengths to normal bone length standards, as described by Poznanski et al [1972a] and Garn et al [1972]. The method provides a quantitative assessment of the amount and direction of abnormality of the hand skeleton. MCP analysis has been used in numerous syndromes [Poznanski et al, 1972b; 1973; Poznanski, 1974; Escobar and Bixler, 1977; Halal and Preus, 1979; Butler et al, 1982; Kaler et al, 1982].

Recently, we derived a method of MCP analysis for 16 patients diagnosed with Sotos syndrome to evaluate its potential as an additional diagnostic technique in this condition.

MATERIALS AND METHODS

MCP Data

Postero-anterior hand radiographs were obtained on 16 individuals diagnosed with Sotos syndrome. The diagnosis of Sotos syndrome was made by at least two physicians on more than one occasion. This group included 11 males and 5 females ranging in age from 8/12 to 13 8/12 years, with a mean age of 5 4/12 years.

The metacarpophalangeal bone lengths of each patient were measured in millimeters with a vernier caliper and compared to bone length standards (appropriate for age and sex) published by Garn ([1972], white Americans, age 2 years to adulthood) and Poznanski ([1974], Gefferth Hungarian sample, birth to 15 months). Through these comparisons, Z score values for the 19 bones of each patient were obtained ($Z \text{ score} = \frac{\text{observed bone length} - \text{mean bone length}}{\text{standard deviation}}$ associated with the particular age and sex of normal standards). Therefore, MCP on a given patient is the set of 19 Z scores, which may be plotted on a graph or subjected to various statistical methods for study and comparison with the MCP of other patients, or groups of patients [Poznanski et al, 1972a].

Correlation Studies

A “mean” pattern profile, based on the average Z score for each bone, of 16 patients was derived [Poznanski et al, 1972a; Garn et al, 1972]. The pattern of each patient was compared to this mean pattern and to each other via a correlation program which produces a Pearsonian r value (correlation coefficient).

Discriminant Analysis

A forward stepwise method of discriminant analysis [Enslein et al, 1977] was performed on the 19 Z scores and the age of individuals from two groups: the 16 patients with Sotos syndrome and a control group of 41 normal subjects whose hand radiographs were randomly

obtained from the records of Indiana University School of Dentistry, Department of Orthodontics. The 41 normal individuals included 17 males and 24 females, with an age range of 9 6/12 to 18 years and a mean age equal to 13 1/12 years.

RESULTS

The mean pattern profile based on the 16 patients with Sotos syndrome contains one major peak in the proximal phalangeal area (Fig. 1). The mean Z scores fall between 1.5 and 3.5. Any Z score of 0.5 or higher is significantly different from zero; therefore, each measured hand bone is significantly longer than the mean for normal individuals at the 5% level. From the profile, it appears that the distal hand bones are relatively short compared to the proximal bones.

Next, the correlation program was used to assess similarity between the mean pattern and each of the 16 individual patterns. Twelve of 16 individuals had significant positive correlations (Table I). In a correlation matrix of Sotos syndrome patients, 91 of 241 correlations were significant ($P < .05$).

Discriminant analysis of the normal and Sotos syndrome cases resulted in a discriminant function based on 2 of the 19 MCP variables and age. In the discriminant analysis, patients with Sotos syndrome were distinguished from the normal individuals at an overall correct classification rate of 100% for our sample (Fig. 2). The two MCP variables in the discriminant function were the Z scores representing (1) the third proximal phalanx (X_8) and (2) the second middle phalanx (X_{11}).

DISCUSSION

Large hand size is a recognized characteristic of individuals with the Sotos syndrome. The mean pattern profile based on our 16 patients confirms this characteristic in quantitative terms. The correlations in Sotos syndrome individuals suggest a pattern of homogeneity with 75% of the individuals possessing a significant correlation at the 5% level. Therefore, a particular hand profile for Sotos syndrome apparently exists as suggested by Halal [1982].

No significant positive or negative correlations were found when comparing the individual MCP variables and age. Therefore, growth in hand size does not seem to accelerate significantly with age, as in the Prader-Willi syndrome, in which MCP variables are negatively correlated with age, indicating a slowing-down of hand growth relative to that of normal individuals [Meaney and Butler, 1983].

The discriminant analysis results suggest that effective delineation of Sotos syndrome patients from normal individuals is possible on the basis of MCP data. We are encouraged by these results especially since the hand x-rays of several individuals were obtained at a young age before the diagnosis was clearly established. Additional testing with a larger sample size is needed to test the power of the discriminant method to distinguish patients with Sotos syndrome not only from a normal sample but from patients with other conditions featuring large hands and/or a generally similar phenotype. The observations presented in

this report suggest the potential of MCPP analysis as a diagnostic tool in the evaluation of patients in whom Sotos syndrome is suspected.

Dr. John Opitz has suggested that cerebral gigantism may be a sequence and not a syndrome. The pattern of multiple anomalies including macrocephaly, craniofacial abnormalities, mental retardation, language deficits, and large size may not be a syndrome but, rather, be derived from a single anomaly such as an enlarged cerebrum. This is an interesting suggestion, and further research is needed for clarification.

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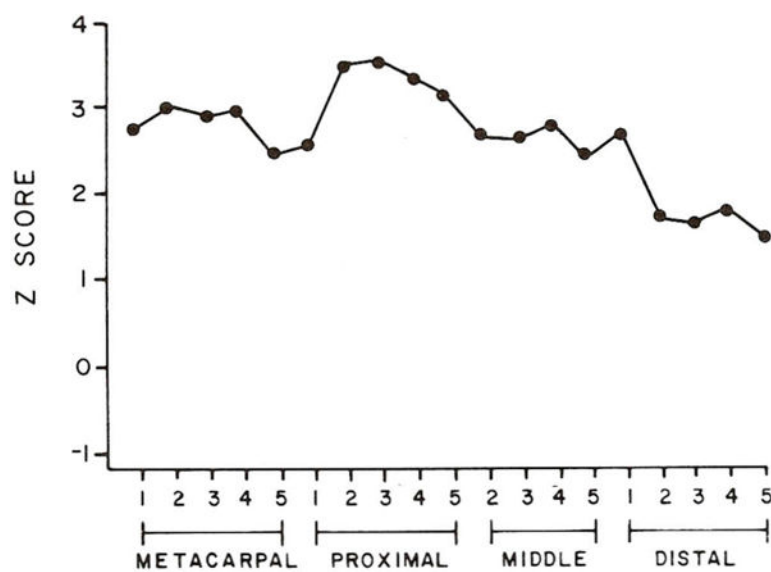


Fig. 1.
Mean MCP for 16 individuals with Sotos syndrome.

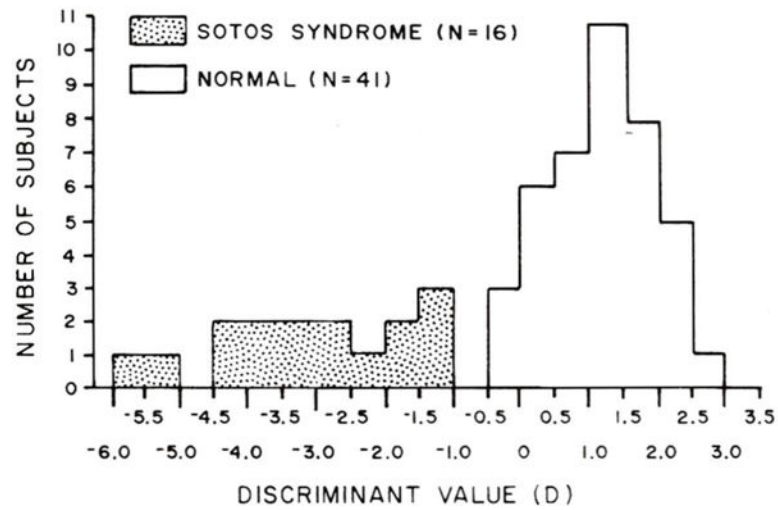


Fig. 2.

Histogram depicting normal and Sotos syndrome classification by discriminant analysis. $D = -2.24 - 0.92(X_8) + 0.41(X_{11}) + 0.24(\text{age in years})$.

TABLE I

Correlations Between Sotos Syndrome Individual's MCPP and Group Mean MCPP

Age (yrs)	Sex	Correlation
7.3	M	-0.04
2.2	M	0.74 ^{**}
8.3	F	0.41 [*]
2.1	M	0.84 ^{**}
3.4	M	0.88 ^{**}
5.0	F	0.34
1.7	M	0.88 ^{**}
1.2	M	0.47 [*]
10.0	F	0.69 ^{**}
3.2	M	0.62 ^{**}
5.0	M	-0.06
6.0	F	-0.19
13.8	M	0.59 ^{**}
0.8	F	0.48 [*]
4.6	M	0.49 [*]
12.1	M	0.78 ^{**}

^{*} P < .05 for one-tailed test.

^{**} P < .005 for one-tailed test.